ASSESSING THE POTENTIAL OF ADENOVIRAL VECTORS FOR GENE TRANSFER TO BRAIN. *D. Ingram, H. Ikari, H. Kuo, L. Ziang, J. Chernak, E. Spangler, G. Roth,* Gerontology Research Center, NIA, NIH, Hopkins Bayview Campus, Baltimore, MD 21224, *and R. Crystal, A. Mastrangeli.* Div. Pulmonary & Critical Care Medicine, Cornell U. Medical School, New York, NY 10021

The use of viral vectors is emerging as a viable method for intracerebral gene transfer. Adenoviral (Ad) vectors present several advantges for such approaches because they can (a) be rendered replication deficient; (b) be modified to accept large DNA pieces; (c) be produced in high titers; (d) provide extrachromosomal nuclear incorporation; and (e) lack association with human neoplasms. We are exploring in rat brain several applications for Ad vectors including their viability and transportability in the CNS and their ability to transfer genes for neurotransmitter receptors. We have observed long-term viablity (up to 4 weeks) of vectors coding for a reporter gene, *lacZ*. In addition, we have observed retrograde transport of such Ad vectors to distal loci where the reporter gene shows distinct evidence of protein production evidenced by β-galactosidase (βgal) histochemistry. For example, injections of Ad vector into the striatum results in highly distinctive staining of the dopamine (DA) producing substantia nigral cells containing tyrosine hydroxylase. Such demonstrations show potential for using Ad vector in retrograde tracing studies. We have also observed transport of an Ad vector through the ventricular system to a lesion site. Specifically, we have injected a vector containing *lacZ* into lateral ventricle and observed βgal staining in the contralateral cortex damaged by a photothrombotic stroke. This finding demonstrates the potential for carrying neuroprotective and trophic genes to damaged brain sites. We have also produced an Ad vector containing the cDNA for the rat dopamine D_2 receptor. In both *in vitro* and *in vivo* studies, this vector can produce protein which binds ligand. Studies to assess behavioral function involve unilateral injections of the vector into rat striatum to determine if apomorphine (a dopamine agonist) can induced stereotyped rotation. Thus far, results have been inconsistent. However, it is clear from this work and others that Ad vectors offer many opportunities for gene therapy in the CNS.